

CLAIMS

1. Non-human transgenic animal, being transgenic for having altered melusin expression.
2. Non-human transgenic animal according to claim 1,
5 characterized in that said altered melusin expression is performed by stable or transient modification of melusin expression at transcriptional, translational or post-translational level.
- 10 3. Non-human transgenic animal according to claim 1 or 2, characterized in that said altered melusin expression is an inactivation of melusin gene.
4. Non-human transgenic animal according to claim 3,
15 characterized in that said gene inactivation is performed by genetic approaches.
5. Non-human transgenic animal according to claim 4,
characterized in that said genetic approaches are selected from the group consisting of homologous recombination, antisense RNA or DNA and RNA or DNA
20 interference approach.
6. Non-human transgenic animal according to any of the preceding claims, characterized in that said animal is a melusin-null transgenic animal.
7. Non-human transgenic animal according to any of the
25 claims 1 to 6, characterized in that said animal is subjected to hypertensive condition.
8. Non-human transgenic animal according to claim 7,
characterized in that said hypertensive condition is determined by surgical operation.
- 30 9. Non-human transgenic animal according to claim 8, characterized in that said surgical operation consists in surgical constriction of the transverse aorta.
10. Non-human transgenic animal according to claim 7,
35 characterized in that said hypertensive condition

is determined by pharmacological treatment, preferably with hypertensive drugs.

11. Non-human transgenic animal according to claim 7, characterized in that said hypertensive condition is determined by high sodium diet.
12. Non-human transgenic animal according any of the preceding claims, wherein said animal develop at least impaired heart hypertrophy.
13. Non-human transgenic animal according any of the preceding claims, wherein said animal develop at least heart dilation.
14. Non-human transgenic animal according any of the preceding claims, wherein said animal develop at least heart failure.
15. Non-human transgenic animal according any of the preceding claims, wherein said animal is a mammalian.
16. Non-human transgenic animal according to claim 15, wherein the mammalian belongs to the murine genus (*mus musculus*).
17. Non-human transgenic animal according to claim 16, wherein said mouse belongs to the 129SV, C57B1 or 129SVxC57B1 strain.
18. Use of non-human transgenic animal according to any of the preceding claims for the selection of compounds pharmacologically active in the prevention and/or treatment of heart failure.
19. Use of non-human transgenic animal according to any of claims 1 to 17 for the study of heart pathologies, wherein said heart pathologies are selected from the group consisting of: heart failure, congestive heart failure, dilated cardiomyopathy, hypertensive cardiomyopathy, hypertrophic cardiomyopathy, heart infarct.

20. Cells derivable from the non-human transgenic animal according to any of claims 1 to 17 and having altered melusin expression.
- 5 21. Cells according to claim 20, characterized in that said cells carry a mutation inactivating melusin gene.
22. Cells according to claim 20 or 21, characterized in that said cells are lacking melusin expression.
- 10 23. Use of cells according to any claim 20 to 22 for the screening of compounds pharmacologically active for the prevention and/or treatment of heart failure.
- 15 24. Method for the preparation of a non-human transgenic animal according to claim 1 comprising essentially the steps of:
- i) preparing a non-human transgenic parent animal carrying an inactivated melusin allele;
 - 20 ii) breeding the parent transgenic animal with a non transgenic animal;
 - iii) selecting transgenic animals heterozygote for the melusin gene mutation.
- 25 25. Method according to claim 24, further comprising the step of iv) breeding the heterozygote transgenic animals to select homozygote transgenic animals for the melusin gene mutation.
26. Non-human animals in which melusin function has been inhibited by the use of natural or synthetic compounds.
- 30 27. Use of the animal according to claim 26 to study the impaired cardiac hypertrophy.
28. Use of the animal according to claim 26 to study cardiac dilation.
- 35 29. Use of the animal according to claim 26 to study the heart failure.

- 5 30. Method for screening compounds able to interact with melusin binding proteins, said compounds being pharmacologically active in the prevention and/or treatment of heart failure, wherein said method comprises using melusin, fragments and/or derivatives thereof.
- 10 31. Method for screening compounds able to interact with melusin, said compounds being melusin agonists and pharmacologically active in the prevention and/or treatment of heart failure, wherein said method comprises using melusin, fragments and/or derivatives thereof.
- 15 32. Use of melusin, fragments and/or derivatives thereof for the manufacture of a medicament for the prevention and/or treatment of heart failure.
- 20 33. Use of melusin, fragments and/or derivatives thereof for the screening of compounds pharmacologically active for the prevention and/or treatment of heart failure.
- 25 34. Use according to claim 33, characterized in that said pharmacologically active compound is a melusin agonist.
- 30 35. Use according to claim 33, characterized in that said pharmacologically active compound is able to interact with melusin-binding proteins.
36. Use of a DNA vector for the manufacture of a medicament for use in the prevention and/or treatment of heart failure, said vector comprising a transgene coding for the melusin protein or fragments thereof and expressing said transgene in the myocardium.
37. Use according to claim 36, characterized in that said transgene comprises melusin cDNA or fragments thereof.

38. Use according to any claim 36 to 37, characterized in that said vector is an adenoviral vector or a lentiviral vector.
- 5 39. Pharmaceutical compositions comprising melusin, fragments and/or derivatives thereof for the prevention and/or treatment of heart failure.